Hypophysectomy; ground breaking treatment for acromegaly in cats - an overview of cutting edge surgery

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ABSTRACT: Acromegaly is a condition caused by a pituitary somatotroph adenoma which causes an over production of somatotropin (hypersomatotropism). This can cause the patient to become insulin resistant and therefore suffer from uncontrolled diabetes. The hypophysectomy is a ground breaking surgery. It can effectively treat feline acromegaly caused by a pituitary somatotroph adenoma by removing the pituitary using a transoral transphenoidal approach (through the roof of the mouth).

Keywords: Hypophysectomy; acromegaly; hypersomatotropism

Introduction

Several specific pathological conditions can result in hypersomatotropism, the excess production of the growth hormone, somatotropin, as well as insulin-like growth factor 1, or IGF-1. The over production of both of these hormones causes many different side effects and chronic over exposure can lead to a condition known as acromegaly. Although it is not a common condition, research shows that it is a potentially underdiagnosed endocrinopathy in diabetic cats (Niessen et al., 2007). Acromegaly is now an important differential in insulin resistant cats. Research has shown that somatotropin is an important modulator of insulin sensitivity so excess somatotropin can induce insulin resistance as well as evident diabetes mellitus. The direct effects of somatotropin can include lipolysis and restricted cellular glucose transport (Dominici, Argentino, Muñoz, Miquet, & Sotelo, 2005). Impaired glucose tolerance and insulin resistance resulting in diabetes mellitus are seen in all cats with acromegaly (Niessen et al., 2007).

In cats, acromegaly is usually caused by a tumour (adenoma) of the pituitary gland, specifically the pars distalis area which contains somatotropin secreting cells (somatotrophs). This causes an over secretion of the growth hormone. Organomegaly including renomegaly, hepatomegaly, and enlargement of the endocrine organs is common alongside enlargement of extremities, body size, jaw, chin, nose and skull (see **Figures 1a** and **b**). Stridor is evident due to increased tissue mass around the airway. Acromegaly can also affect the heart and cardiomegaly may be evident. If left untreated, progression to congestive heart failure may occur (Niessen, Peterson, & Church, 2012).

Feline acromegaly is more prevalent in older, male cats with an age range of 8–14 years (Niessen et al., 2007).

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Figure 1. a & b: 2 confirmed acromegalic cats pre hypophysectomy surgery. Note the enlargement of the nose and chin (photos authors own).

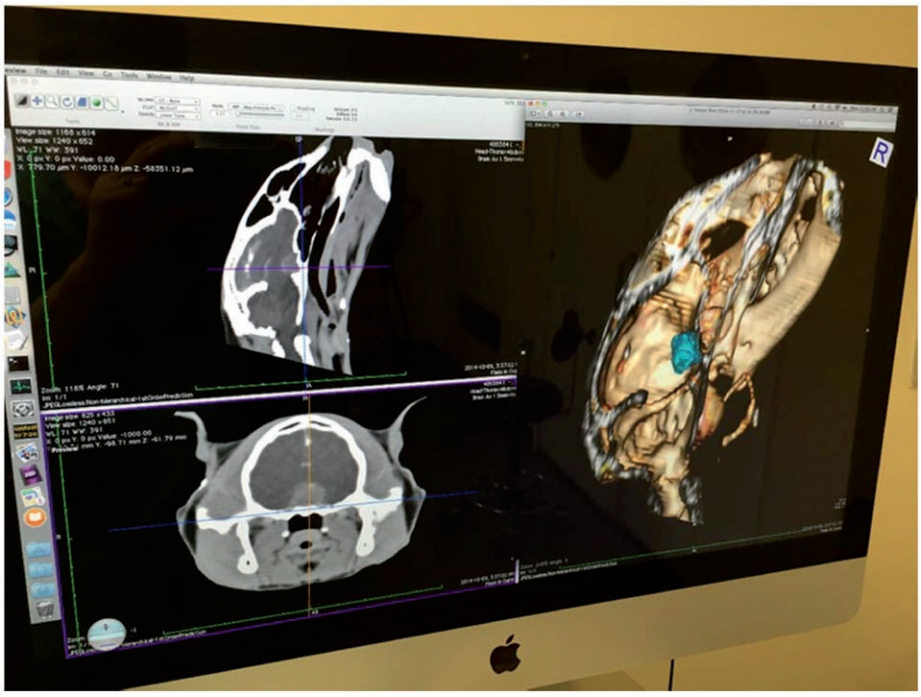

Figure 2. Using CT to show the position of the pituitary mass (photo by Joe Fenn).

Treatments that are available for acromegaly include radiation therapy of the tumour, medical treatment using pasireotide LAR (long acting release), which is a long acting somatostatin multireceptor ligand which has shown to be the first drug to show potential as a long-term management option for diabetic cats with acromegaly where surgery may not be an option. A recent study (Gostelow et al., 2017b) found pasireotide LAR treated cats showed a significantly decreased IGF-1, improved insulin sensitivity, with some cats achieving diabetic remission. However diarrhoea was seen to be a significant adverse effect along with increased polyphagia.

The permanent solution is a hypophysectomy which is the surgical removal of the tumour via neurosurgery. A hypophysectomy patient requires close monitoring post-surgery and hormone replacement via eye drops and oral medications. Careful glucose monitoring and controlled insulin treatment is required. The veterinary nurse plays a vital role here as the recovery period for the cats is intensive and they require a lot of skilled nursing care. This article explains the authors experience with this surgery and how the veterinary nurse plays a pivotal role in the treatment and recovery of these patients.

Preparation for surgery

Prior to being admitted for surgery, the cat will already have had a diagnosis of acromegaly confirmed with a CT scan and IGF-1 and fructosamine blood tests. Once confirmed, discussions are had with the owner about whether surgery will be beneficial for the cat, taking into account the cats current health, any other health concerns, the owners wishes and any financial constraints the owner may have. An IGF-1 measurement of >1000 ng/ml is suggestive of acromegaly. The CT scan looks for a growth on the pituitary gland (see **Figure 2**) which indicates acromegaly as well as ruling out any other medical issues which may mean the cat is an unsuitable candidate for surgery, or issues that need further investigating prior to surgery. A heart scan is also performed as acromegaly can cause enlargement of the heart muscle and the heart needs to be healthy in order to cope with the surgery. A blood test to determine blood type is carried out so the blood donor team can prepare a donor if needed. Cats are admitted 3–4 days prior to their scheduled surgery to allow time to acclimatise to the hospital environment and allow for any further tests that may need to be done prior to the surgery. The cat will continue to receive its normal insulin dose and food until the morning of the surgery.

Induction for surgery

The cat is starved for around 12 hours before surgery and receives a half dose of its morning insulin. At induction, blood glucose levels are checked alongside other vital parameters (gases, electrolytes, packed cell volume and total solids). This is so there is something to refer back to during the surgery and post surgery. An intravenous catheter is placed in the cephalic vein to allow for induction of anaesthesia. The cat is intubated and the endo tracheal tube is inserted and bound to the lower jaw curving the tube to the right, behind the right canine as the incision for the surgery occurs through the soft palate. Intravenous fluids are started using NACL 0.9% and most cats will need to be placed on a CRI of soluble insulin during surgery. A long stay intravenous catheter is placed usually in the saphenous vein to allow for drawing of blood during surgery. Due to the surgery being performed through the roof of the mouth, broad spectrum antibiotics are

started with amoxycillin-clavulanate acid due to its good activity against likely oral or respiratory tract contaminants, at a dose rate of 20 mg/kg intravenously and buprenorphine is given at a dose of 0.01–0.02 mg/kg for analgesia. The fur is shaved from the top of the head to allow for placement of the head brace. This area is prepped using a preoperative skin preparation containing chlorhexidine gluconate and isopropyl alcohol. The cat is then ready to be transported to theatre (see **Figure 3**).

Figure 3. In induction, prepping the cat for the move to theatre (photo by Joe Fenn).

The surgery

When in theatre, the cat is placed in sternal recumbancy with the head facing the surgeon. A surgical head brace is used with pins in contact with the parietal bone to maintain the head elevation (see **Figure 4**). The oral cavity is prepped using a povidine iodine solution at a dilution rate of 1:50. The pituitary is to be accessed by a soft palate incision (transphenoidal transoral approach) followed by incision and retraction of the mucoperiosteum overlying the basisphenoid and presphenoid bones. The bone overlying the pituitary is then removed by burring to allow access to the pituitary fossa and gland. Pre-operative CT (computed tomography) imaging is used with bone landmarks such as the hook of the hamular process of the pterygoid bones to determine the site to burr (see **Figure 5**). Once durotomy occurs, a constant rate infusion of hydrocortisone sodium succinate is started due to disruption of the pituitary. The pituitary also releases adrenocorticotrophic hormone which stimulates the adrenals to release cortisol so a form of cortisol must be administered. DDAVP or demopressin is also given. This is a synthetic replacement for vasopressin otherwise known as anti-diuretic hormone. This hormone is released by the pituitary and it has an important role as it helps prevent loss of water from the body by reducing urine output and helping the kidneys reabsorb water into the body. Vasopressin also raises blood pressure by narrowing blood vessels. Blood glucose checks are taken every 30 min and blood gases, PCV and TP every 2 hours during surgery. Once the dura mater is incised and the pituitary gland is exposed, the pituitary gland is gently extracted (see **Figures 6** and **7**). Some leaking of cerebrospinal fluid and haemorrhage may occur at this point, and this is stopped using cotton buds and haemostatic collagen fleece. The drill hole is closed using haemostatic collagen and surgical adhesive and the soft palate is closed using absorbable suture material in two simple interrupted layers. The site of entry of the head brace pins onto the skull are closed with simple interrupted sutures which are removed when the skin has healed.

Figure 4. Positioning using surgical head brace (photo by Joe Fenn).

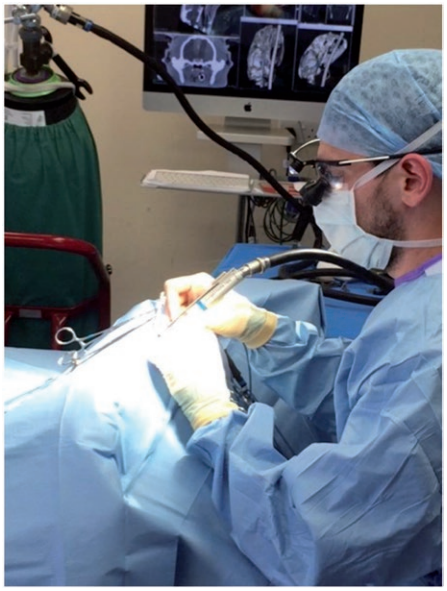

Figure 5. Drilling of the bone overlying the pituitary (photo by Joe Fenn).

Risks of the surgery can include bleeding on the brain, blood pressure problems and electrolyte imbalances peri surgery, and blood pressure problems, electrolyte imbalances and palate wound dehiscence post surgery. A possible concern during surgery may be that the mouth is kept open in order to access the pituitary. A study showed the use of spring-loaded mouth gags in cats can be associated with the development of central neurological deficits, including blindness due to the maxillary arteries becoming compressed as a result of constant force from the mouth gag (Martin-Flores, Scrivani, Loew, Gleed, & Ludders, 2014). During this surgery however, the mouth is kept open using surgical tape and there is not a constant force applied to the cats mouth so the risks appear to be minimal.

Recovery

Once the surgery is completed, the cat is sent for a CT to check that all the tumour

Figure 6. Bone defect following removal of the pituitary mass (photo by Joe Fenn).

Figure 7. The excised pituitary gland (photo by Joe Fenn).

has been removed, then a jugular central line is placed in order to allow for easy blood sampling and drug administration during the recovery period. The cat is then taken to the intensive care ward for one to one care and intensive monitoring. A blood glucose monitor called a Guardian is placed on the cat, this is a monitor that constantly checks blood glucose levels without the need for ear pricks or venepuncture. During the cats time in ICU (see **Figures 8a** and **b**), insulin is continued under the instruction of the primary clinician and insulin dosage altered taking into account the blood glucose readings. Prozinc is used as an insulin as a recent study proved it to produce better glycaemic control and higher remission rates (Gostelow et al., 2017a). Analgesia (buprenorphine) is given accordingly along with intravenous fluid therapy. Antibiotics (amoxycillin-clavulanate acid) are continued intravenously then orally once the cat is

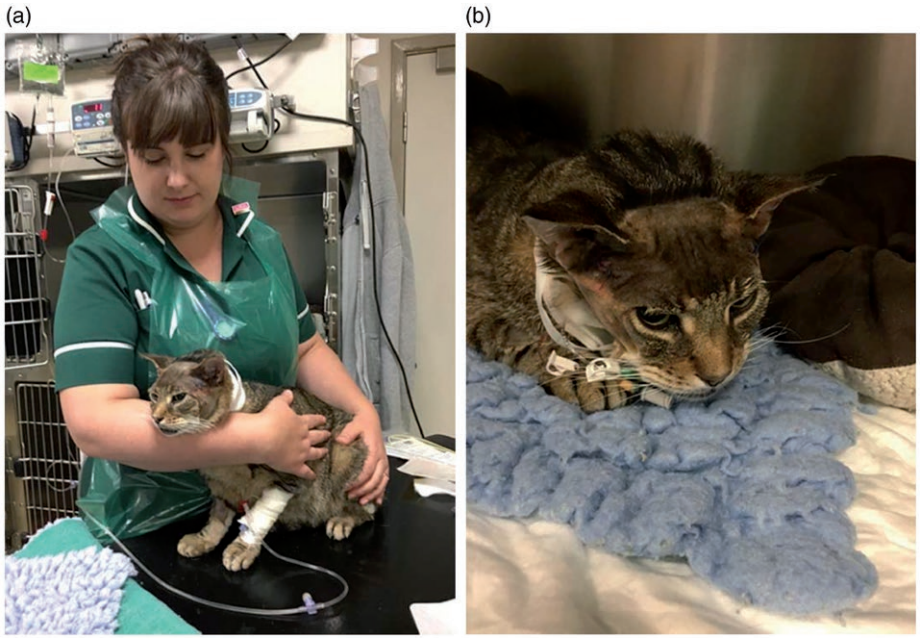

Figure 8. a & b: Cat day 1 post hypophysectomy (Photos authors own).

eating, to avoid infection, this is all the more important due to the surgery being performed in the mouth. Hydrocortisone is continued intravenously until the cat is able to take the medication orally, demopressin is given as DDAVP into alternate eyes every 8 h, and a thyroid replacement (thyroxine) is given orally. In 80% of cases, DDAVP can be stopped after a few months. Amoxicillin is stopped after 2 weeks. Once the cat is deemed stable enough it returns to cat ward, where less intensive nursing will then continue. This is normally after a couple of days. The effects of the surgery can normally be seen within 1 week and up to a couple of months as the cat becomes more responsive to the insulin given and subsequently, hopefully goes into diabetic remission. In a study looking at the hypophysectomy surgerys carried out at the Royal Veterinary College in 2015 when 21 cats had been operated on, the percentage of cats seen to achieve diabetic remission was 78%. The remaining cats went on the achieve excellent glucaemic control using insulin (Kenny et al., 2015). The hospital has now operated on over 68 cats.

Complications that can occur during this recovery time can include pain and inflammation around the sight of the surgery and also where the head is placed in the brace, infection, and electrolyte imbalances. As noted in the study carried out after the Royal Veterinary College had operated on 21 cats, 2 cats did not recover from the anaesthesia and 1 was euthanised 17 days post operatively due to septic meningitis. Other complications seen were paresis of the left orbicularis oculi muscle in 2 cats, one of which was one that died and in the other cat it resolved, cardiac arrest occurred in 1 cat post-operatively during jugular catheter placement, but this cat was successfully revived and recovered. One cat developed a left pelvic limb monoparesis, which improved but not fully. Palatal wound breakdown was not seen in any of the cats operated on (Kenny et al., 2015).

Conclusion

There seem to be many uncontrolled diabetic cats that are actually suffering from undiagnosed feline hypersomatotropism, or acromegaly. Acromegaly is a relatively new and often under discussed concept in veterinary medicine and the surgical treatment for it using the hypophysectomy at the moment limited to a very minimal amount of veterinary centres. Routine screening of diabetic cats using IGF-1 should be considered to gain early detection of acromegaly. Previous treatments have included radiotherapy and medical treatment with somatotrophin inhibitors, however the permanent surgical solution, the hypophysectomy has proven to be a much superior choice of treatment with radiation therapy being frequently ineffective. Hypophysectomy surgery as a treatment for feline hypersomatotropism has shown to result in a high incidence of diabetic remission and resolution of acromegaly.

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